Improvement of Intestinal Mucosa and Flora

7.1. Introduction

The gastrointestinal tract and its symbiosis with micro-organisms has been an issue amongst physicians and researchers alike. In the past, intestinal micro-organisms (bacteria and fungi) have been considered to be detrimental to the human host. Recently, research has shown that the flora plays an important role in the vitality of the human host.

In the body, the intestinal mucosa forms the largest contact surface with the outer world (skin 2 m^2; lung 100 m^2; gut 500 m^2). The intestinal tract forms an open functional system with about 300-500 m^2 active resorption surface for nutrients, water, bile salts and secretions by glands within the gut for protection against micro-organisms and dangerous antigens and toxic material. Also, the gut excretes IgA and waste products into its lumen.

7.2. Microbiology of the gut

In total, it is estimated that in an average adult, there are about 1000 trillion (10^{15}) bacteria living in the gut, mainly in the colon. This is 100 times more than the total amount of cells in the adult human body. The gut flora contributes about 700 grams to the total body weight. At birth, the gut is sterile. The colonisation of the gut is an ongoing process and can be divided into four stages.[i],[ii]

1. Phase I: initial colonisation through ingestion of mainly aerobic bacteria (*E. coli*, *Enterococcus*, etc.) from the mother during the birth process;
2. Phase II: establishment of the early flora from the second week post partum on. Now, the gut is colonised by micro-organisms which break down complex carbohydrates, and aerobic and anaerobic bacteria (*Lactobacilli*, *Bifidobacteria*). The newborn will ingest and be colonised mainly by bacteria from the mother through direct contact with the skin and through breastfeeding;
3. Phase III: colonisation through micro-organisms from food stuffs other than milk. Usually, these bacteria are anaerobic (*Eubacterium*, *Veillonella*, *Fusobacterium*, *Megasphaera*,*Clostridium*, etc.). At this stage, the adult situation is achieved. There is being established a kind of equilibrium between many of the various micro-organisms;
4. Phase IV: stage of the elderly. In the elderly, there is a shift in the equilibrium between the aerobic and the anaerobic bacteria with an increase of the Clostridium species and a decline of the Bifidobacteria.

The oxygen use of the aerobic bacteria is so high within the gut that anaerobic bacteria live in symbiosis with aerobic bacteria and further break down of what is left of the foodstuffs.

7.3. Importance of the intestinal flora for the human host

The development of the gastrointestinal tract and the immune system is highly influenced by the intestinal flora.[iii],[iv] Therefore, in cancer, allergies, chronic viral

diseases, and other diseases, which are rooted in a malfunctioning of the immune system (immune deficiencies), the content and quality of the intestinal flora are of utmost importance.

Also, the absorption of many vitamins depends on the intestinal flora, like Vitamin K, and several of the Vitamin B group (B1, B2, B6, B12), folic acid, biotin, niacin, pantothen acid.[v]

7.4. Importance of the intestinal flora for the development and functioning of the Gut Associated Lymphoid Tissue (GALT)

With food intake, many potentially infectious microorganisms and detrimental toxins (antigens) enter the gastrointestinal tract. In the submucosal layers of the gut, well-developed lymphoid tissue (the Gut Associated Lymphoid Tissue or **GALT**) is present to prevent invasion of abnormal microorganisms and toxins. In no other organ system, the immune system is so well developed and omnipresent as in the gastrointestinal tract. The plaques of Peyer are a good example of GALT. Within the lymphocyte population, especially T-lymphocytes in the mucosa and the *lamina propria* play an important role in preventing a systemic immune reaction to food antigens (oral tolerance). In case of food allergies, but also the initiation of allergies over the mucosa, like in hay fever and contact allergies, there is a dysfunction or deficiency of GALT. Therefore, in case of allergies, other than triggered by intake of certain foodstuffs, the intestinal flora should be examined as well.

Under physiological conditions, plasma cells in GALT synthesize and excrete IgA into the lumen of the gut. In contrast to all other classes of immunoglobulins, IgA is resistant to many endogenous and bacterial proteases, and cannot be broken down after it has been excreted into the lumen. IgA works like antibody painting and protects the mucosa from invasion of detrimental microorganisms and toxins. In other words, IgA is the first line of defense.[vi]

Diet has a definite influence on the functioning of GALT (see Chapter 6. Orthomolecular Therapy. Therefore, in the *Cologne Model*, attention is given to diet and intake of trace elements, vitamins and cancer-protective plant substances, like phenols, flavonoids, etc.

A proper development of the immune system in the gut and a balanced intestinal flora will add to health and its maintenance. In case of (chronic) disease, particular attention must be paid to the composition of the various bacterial subpopulations within the gut.

In the *Cologne Model*, preventive medicine also plays an important role. Therefore, attention is paid to the composition of the intestinal flora as well, as, over time, a misbalanced flora can add to the risk of developing cancer, allergies and chronic disease.

7.5. Therapeutic strategies and interventions

There are three main considerations regarding therapeutic interventions:

1. Is the current illness directly connected with the barrier function of the gut?

2. Does the current illness have a direct effect on the intestinal flora?
3. Can the course of the current illness positively be influenced through affecting the intestinal flora?

7.5.1. Change of the milieu

Micro-organisms have a tremendous flexibility in the physiology of their metabolism, compared to plants and animals. In part, this is due to their tiny dimensions. On average, a bacterium contains less than 100,000 protein molecules. If, at a given time, certain enzymes are not needed, they are just not produced. Micro-organisms have a tremendous metabolic (anabolic) potential. A cow of 500 kg produces per day approximately 1 kg protein. Under perfect circumstances, 500 kg of micro-organisms could produce more than 10,000 kg of protein in the same time.

The pH of the intestinal milieu plays an important role in the metabolism and reproduction potentials of micro-organisms. The optimal pH of the gut (colon) is <7.0. Usually, in chronic disease and cancer, the pH is clearly >7.0. Therefore, in these cases, the pH of the milieu must be lowered. This can be brought about by dietary changes, like increasing the intake of fibre and lactulose, and of *Lactobacilli*, and decreasing the intake of proteins.

Fibre and lactulose are usually plant derived and consist of a mixture of cell membranes and cellulose, which cannot further be broken down by the human digestion processes. A fibre-rich diet lowers blood cholesterol and stimulates peristalsis. Through increasing gut motility, passage of food rests (*faeces*) is hastened and thus, toxic substances, among them bile salts, free ammoniac, psychopharmaca and antibiotics, have less contact with the intestinal mucosa. Thus, in this way, it can be understood that fibre rich nutrition lowers the risk of colon cancer.[vii]

7.5.2. Reduction of protein intake

Some of the dietary proteins reach the colon. Here, bacteria, which can break down proteins, are available. Among them are various *E. coli* and *Klebsiella* and *Proteus* species. Through proteolysis, free ammonia and amines are formed, which make the milieu of the gut more alkaline (ph >7.0). Therefore, dietary intake of proteins should be modest. Usually, a vegetarian diet is rich in fibre and relatively low in protein.

7.5.3. Value of Lactobacilli supplementation

Bacteria like *Bifidobacilli* and *Lactobacilli*lower the pH of the colon and can be an adjunct therapy in the treatment of cancer patients and patients who received prolonged antimicrobal therapies.

The efficacy of selected probiotics for prophylaxis and treatment of chronic inflammatory, infectious, and allergic diseases has been confirmed by randomized controlled clinical trials. The E. coli strain "Nissle 1917" decreases relapse rates in patients with ulcerative colitis, and the probiotic mixture VSU3 was found to lower the incidence of pouchitis. Both Lactobacillus rhamnosus GG and Saccharomyces boulardii are effective for the treatment and prevention of infectious diarrhea in infants and children and of antibiotic-associated diarrhea. In addition, Lactobacillus

rhamnosus GG can prevent allergic disease in newborns when administered in the perinatal period. So far, the mechanisms of action and pharmacokinetics of probiotic drugs are unknown. This and the fact that the number and size of clinical trials are limited do not warrant general recommendation of the mentioned probiotics for treatment of selected diseases. However, probiotics are a valuable and effective alternative treatment in selected cases. By contrast, the relevance of prebiotics, synbiotics, and probiotic foods for the prevention and treatment of diseases remains to be established. Modulation of gut flora and intestinal barrier functions by pro- and prebiotics is a research field that opens new insights into the pathophysiology of immune-mediated, food-related, and infectious diseases of the intestine and outside the intestine.

7.5.4. Immunomodulation through microbiological interventions

Fundamentally, any immunomodulation through therapeutic intervention only makes sense in diseases, where the cause of the disease lays within the immune system itself, or where through medical interventions (antimicrobal therapies), the intestinal flora has been severely altered. One parameter is the IgA concentration in the stool.7

Through application of commercially available microbiological preparations, the milieu of the intestinal lumen can be influenced positively, and thus, an effect on GALT can be achieved.

In this context, *Saccharomyces boulardii* plays a special role in immunomodulation and improvement of the milieu of the intestinal lumen.[viii],[ix]*Saccharomyces boulardii* can be given prophylactically in case of antimicrobal therapy to prevent diarrhoea, etc., or to treat imbalances of the flora after such a therapy.[x]

7.6. Pancreas insufficiency

In chronic disease, the exocrine function of the pancreas can become insufficient. Often, this condition is diagnosed late or never. If an insufficiency of the exocrine function of the pancreas is suspected, in the *Cologne Model*, cancer patients are tested for their pancreas function, and substitution of pancreatic enzymes is initiated when an insufficiency has been diagnosed.

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